Fragment Based Drug Discovery

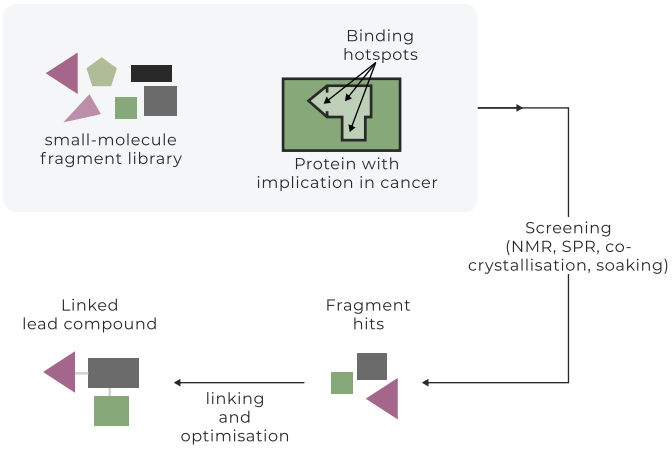
Unlock the Potential of Undruggable Targets...

Fragment-based drug discovery has emerged as a revolutionary approach to identifying novel chemical starting points for a wide range of biological targets, including those once considered undruggable.

By utilising smaller, basic building blocks known as fragments, this cutting-edge method offers unique advantages in the search for potent drug candidates.

Why Fragments?

Fragment-based drug discovery (FBDD) is an established complementary approach to high-throughput screening (HTS). Contrary to HTS, where large libraries of drug-like molecules are screened, FBDD screens involve smaller and less complex molecules which, despite a low affinity to protein targets, display more 'atom-efficient' binding interactions than larger molecules. Fragment hits can, therefore, serve as a more efficient start point for subsequent optimisation, particularly for hard-to-drug targets. Since the number of possible molecules increases exponentially with molecular size, small fragment libraries allow for a proportionately greater coverage of their respective 'chemical space' compared with larger HTS libraries comprising larger molecules.



Our Approach

o2h Med Chemists in conjunction with academic computational chemists have designed the library to ensure pharmacophore diversity, molecular complexity, and with the necessary physicochemical characteristics. We continue to expand our library and fill in gaps. We utilise Biacore T200 Surface Plasmon Resonance (SPR) as a primary screening modality to efficiently evaluate fragments for direct binding at high micromolar concentration and subsequently, fragments with confirmed activity are validated in orthogonal experiments such as thermal stability (TS). If required we can also plugin support for your X-ray Crystallography and NMR.

> *"We have worked with the o2h team on a range of synthetic projects and had consistently positive experience. The combination of competence, effective project management and detailed documentation made us go back again and again."*

-Professor Kirill Alexandrov,
CSIRO, QUT Synthetic Biology Alliance

QUT

Our Development Strategy

Our SPR assay development team follows a meticulous experimental design strategy:

- Target immobilisation based on literature precedence
- Buffer scouting and direct binding with preferred natural peptides or control compounds
- Competitive displacement or allosteric interaction studies
- Detailed sensorgrams with graphical illustrations of Kd, Kon, and Koff
- Optimization of injection time window for maximum signal response
- Evaluation of immobilised protein stability and target responsiveness

Ascertaining The Future Scaffolds Quality

Initial fragment screening identifies hits with activities >50% of theoretical Rmax, followed by full kinetic characterization. Our approach includes:

- Discrimination between specific and non-specific interactions using suitable controls
- Counter screens against unrelated controls or mutant proteins
- Identity and purity confirmation via LC-MS

Empowering Your Discovery Journey

We can support orthogonal assay validation experiments for better confidence in hit identification such as fluorescence based thermal stability experiments.

Shortlisted fragments can be evolved through:

- "SAR by catalogue" approach for related molecules.
- Design and synthesis of analogues for improved potency.
- Integrated drug discovery services for multi-platform profiling.
- Leverage structural and computational insights to understand lead molecule binding modes.
- Possibility to use site-directed mutagenesis studies to aid SAR elucidation and lead optimization.

Join us on an exciting journey of Fragment-based Drug Discovery with o2h discovery. We're your one stop solution, offering strategic planning and flawless execution to transform innovative pharmaceutical ideas into reality.

Get a Quote:

discovery@o2h.com
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